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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,782	03/30/2001	Thomas Rausch	P/2107-162	7866

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EXAMINER

KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
1638	11

DATE MAILED: 10/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/762,782	RAUSCH, THOMAS
Examiner	Art Unit	
Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on ____.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-13 and 15-21 is/are pending in the application.
 - 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) Claim(s) ____ is/are allowed.
- 6) Claim(s) 1-13 and 15-21 is/are rejected.
- 7) Claim(s) ____ is/are objected to.
- 8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 30 March 2001 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on ____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. ____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10.
- 4) Interview Summary (PTO-413) Paper No(s). ____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: ____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-13 and 15-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims any nucleotide sequence of any plant invertase inhibitor gene or any fragment thereof of any length from any source.

Applicant does not describe any plant invertase inhibitor genes other than the apoplastic tobacco gene.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

3. Claims 1-13 and 17-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for tobacco transformed with an isolated tobacco apoplastic invertase inhibitor coding sequence in sense and antisense orientations, bearing seed with altered seed development and reserve content, does not reasonably provide enablement for all plants transformed with any invertase inhibitor coding sequence showing altered seed development and altered reserve content other than in transformed tobacco. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant broadly claims a process for producing a transgenic plant having a deregulated invertase activity, transformed with an invertase inhibitor gene from any plant and of any sequence or any fragment thereof, whose seeds have modified seed development such that an increased amount of reserve material accumulates when compared to seeds of wild type untransformed plants.

Applicant teaches sense and antisense transformation of tobacco with the gene encoding apoplastic tobacco invertase inhibitor by *Agrobacterium tumefaciens* mediated transformation (page 11 lines 3-7); tobacco cell suspension culture as source of invertase inhibitor polypeptide (page 11 lines 7-8); selection of first generation seeds on kanamycin plates (page 11 lines 9-10);

detection by antiserum of an increase of invertase inhibitor polypeptide in the stamens and ovaries of sense transformants; a decrease of said polypeptide in the stamens and ovaries of antisense transformants; determination of seed dry weight, amount of stored oil, and total protein (page 11 lines 27-28, page 12 Tables 1-3); similar germination time for antisense transformed and wild type seeds and delayed germination for sense transformed seeds (page 13 lines 1-9); prophetic transformation of rape and sunflower with an antisense invertase inhibitor construct to alter the amount of stored oil (page 13 lines 10-18); prophetic transformation of corn, oats, rice, wheat, oats, barley and rye with an antisense invertase inhibitor construct to alter starch content (page 13 lines 19-22); and prophetic transformation of soybean and pea (page 13 lines 22-24).

Applicant does not teach isolation of any invertase inhibitor coding sequences other than a tobacco apoplastic invertase inhibitor sequence and alteration of development in transgenic plants bearing seeds with an increase or decrease in reserve content in any plant species other than tobacco.

An important consideration in genetic engineering for altered starch or protein content by altering gene expression is knowing or determining whether the gene or gene product of interest is under some kind of regulatory control or influenced by additional mechanisms governing metabolic flux (Broun *et al.* PNAS July 31, 2001 vol. 98, pp. 8925-8927; see page 8926 second column, 2nd paragraph).

Further, the isolation of orthologous DNA sequences from other species introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or probes with limited homology. Thus the screen for

orthologous sequences would isolate many genes other than those of interest. The inherent unpredictability in isolation of a homologous sequence encoding the same protein activity is illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for the functional divergence seen across a range of enzymes involved in fatty acid metabolism (Broun *et al.* Science Vol. 282 13 November 1998; Abstract lines 4-6 and p. 1317 column 1, lines 51-56).

Moreover, when considering the likely presence of isoforms of the target gene in polyploidal crop species, uncharacterized with respect to the number of target gene isoforms, the phenotypic character expected from expression of a DNA construct often cannot be reliably predicted. In an example that demonstrates this all too common and unpredictable feature in the art, antisense expression of a *gchs2* gene resulted in only partial reduction of *gchs3* and *gchs1* isoforms of the gene in transgenic *Gerbera hybrida* (Elomaa, P., *et al.*, Molecular Breeding 1996, 2: 41-50 on page 48, column 2 lines 4-10). The unpredictability in metabolic engineering is also exemplified in experiments with transformed potato expressing yeast derived invertase in the cytosol, vacuole, or apoplast of potato leaves, having elevated/deregulated invertase activity, which showed a decrease in photosynthesis as measured by a reduction in both Rubisco activation state, a reduction in the rate of CO₂ assimilation, stunted growth and an increase in solute accumulation in leaves associated with plants undergoing water stress in (Bussis *et al.*, Planta 202:126-136, 1997 on page 126, Abstract, lines 1-18 and page 134, columns 1 lines 52-59 and column 2 lines 1-28).

Because the specification provides no guidance for amplifying using PCR primers comprising conserved regions of invertase inhibitor cDNA, one of skill in the art would be required to optimize PCR conditions to eliminate non specific binding and the artifacts generated thereof. This would comprise adjustments in annealing temperatures, testing different concentrations of Mg and template, and the sequencing of putative clones for each species of invertase inhibitor cDNA amplified to verify the product as an invertase inhibitor. The unpredictability in the art would require screening numerous non-exemplified transgenic plants to test various non-exemplified sense and antisense constructs for effectively modified seed development with reduced or increased levels of invertase inhibitor polypeptide resulting in an increase in reserve material presuming they could ever be obtained in every plant species claimed.

Given the lack of guidance for isolating DNA sequences encoding a plant invertase inhibitor and producing plants with increased reserve levels in the specification that reflect the breadth of the claims, and the unpredictability in the art, undue trial and error experimentation would be needed to practice the invention. Therefore, the invention is not enabled for the scope set forth in the claims.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-13 and 15-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections.

At Claim 1, line 1 "a deregulated invertase activity" is indefinite. It is unclear whether the deregulated activity refers to regulation of gene expression, development, tissue specific expression, circadian gene expression, or of total activity. Further, it is not clear if invertase activity will increase or decrease.

At Claim 1, line 2, "stimulates plant development" is indefinite. It is unclear which part of the plant and which phase comprising the ontogeny of the plant would be effected.

At Claim 1, at line 2, line 5, and line 6 "nucleotide sequence" is indefinite. It is unclear whether the sequence encompasses coding, non-coding sequences or both. The term "nucleotide sequence" should read --nucleotide coding sequence--.

At Claim 1, line 3, "cell suspension culture" is indefinite. It is unclear whether any type of cell is contemplated or a particular species of plant cell.

At Claim 1, line 5, "or is derived" is indefinite. It is unclear what is retained and what is left behind in the derivation.

At Claim 1, line 7, "one regulatory unit" is indefinite. It is unclear whether the term refers to a promoter, a terminator, an enhancer, or an intron and whether it actually functions in a plant.

At Claim 5, line 2, "a nucleotide sequence hybridizing with that" is indefinite. Since hybridizations conditions are not stated any sequence will hybridize to the sequence of interest.

At Claim 5, line 3, "a fragment of one of the two" is indefinite. It is unclear what size of a fragment is intended and the fragment would read upon any DNA sequence given the lack of hybridization conditions as stated supra.

At Claim 8, line 2, "in particular a transcription termination signal" is indefinite. The phrase suggests that it is possible to have the complete process without the termination signal and it is unclear if it is to be included or not.

At Claim 12, line 1 "in particular" is indefinite. It is unclear if a plasmid or a virus are required at all.

At Claim 15, "as well as a part thereof" is indefinite. It is unclear whether the term "as well as a part thereof" is referring to the parts of the method of Claim 1 or the parts of the transgenic plant produced by said method.

At Claim 18, line 1, "a functional nucleotide sequence" is indefinite. It is unclear whether a regulatory or a coding function is intended.

At Claim 20, line 2, "or is derived from" is indefinite. It is unclear what is retained and what is left behind in the derivation.

At Claim 20, line 2, "nucleotide sequence" is indefinite. It is unclear whether a regulatory or a coding function is intended.

At Claim 21, line 2, "nucleotide sequence" is indefinite. It is unclear whether a regulatory or a coding function is intended.

At Claim 21, lines 2-3, "one regulatory unit" is indefinite. It is unclear whether the term refers to a promoter, a terminator, an enhancer, or an intron.

At Claim 21, line 3, "in particular the promoter" is indefinite. It is unclear if the promoter is required at all.

Claim 1 recites the limitation "whereby a plant cell of a plant of the same type or variety" in lines 4-5. There is insufficient antecedent basis for this limitation in the claim. The claim should read --whereby a plant cell of said plant--.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 16-17 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The propagating and cropping material of Claims 16-17 would be first generation seeds, fruit, seed husk, embryo, seedling, callus tissue, cell culture, stem, leaf, and root. For example, in the case of biolistic transformation of maize callus, a single insertion event, the seeds from hemizygous transformants would contain tDNA in half the population while the other half of the seeds would have no tDNA insertions whatsoever. Thus, the claims read on products of nature. See *ex parte Grayson*, 51 USPQ 413 (Bd. App. 1941).

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3, 5-8, 10, 12-13, and 15-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Rausch, T. *et al.*, WO 98/04722 A1.

The claims are broad for the reasons discussed supra. In particular, the claims are drawn to a transgenic plant comprising a vector comprising either a sense or antisense invertase inhibitor cDNA nucleotide sequence or fragment thereof or a sequence hybridizing under unspecified conditions thereto, resulting in an increase in the reserve material in its seeds.

Rausch teaches transformation of a plant with a vector comprising a promoter and an invertase inhibitor nucleic acid from tobacco such that the reserve or storage material, namely sucrose, is increased relative to the untransformed wild type plant (See US Patent 6,384,300 entire Abstract; Figures 1 and 2; and column 7, lines 18-26 and column 8, lines 1-26). The invertase inhibitor nucleic acid would inherently contain a transcription termination signal, as evidenced by the successful transcription and translation. Thus, the reference discloses all the limitations of the instant Claims 1-3, 5-8, 10, 12-13, and 15-21.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 1-13 and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rausch, T. *et al.*, WO 98/04722 A1, in view of Gordon-Kamm *et al.* The Plant Cell, July 1990, Vol. 2, pp. 603-618.

Applicant broadly claims a process for producing a transgenic plant comprising a vector comprising a CaMV35S promoter, invertase inhibitor coding sequence and NOS transcription

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terminator, having a deregulated invertase activity whose seeds have modified seed development such that an increased amount of reserve material accumulates when compared to seeds of wild type untransformed plants.

The teachings of Rausch, T. *et al.*, WO 98/04722 A1 are discussed *supra*.

Rausch, T. does not teach transformation of maize with a construct comprising the CaMV35S promoter and NOS terminator.

Gordon-Kamm teaches transformation of maize using a DNA construct having the CaMV35S promoter and NOS terminator (page 614 column 1, lines 5-17).

It would have been obvious at the time of Applicant's invention to modify the invention of Rausch to substitute plant transformation and regeneration of maize transformed with a DNA construct comprising a CaMV35S promoter and a NOS terminator sequence in order to obtain expression of antisense and sense apoplastic invertase inhibitor coding sequences in maize plants and seeds. One of skill in the art would have been motivated by the teachings common in the art that the transformation of maize was generally successful and that one would have had a reasonable expectation of success of regenerating transformed maize plants and seeds.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-22 of U.S. Patent No. 6,384,300. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are broadly drawn to apoplastic invertase inhibitor nucleic acid sequences and the propagating and cropping material of transgenic plants comprising said sequences. Thus, the embodiments of the inventions of Claims 1-22 of U.S. Patent 6,384,300 B1 fall within the scope of Claims 15-17 of the instant application.

12. All claims are rejected.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Sonya Williams, whose telephone number is (703) 308-0009.

Russell Kallis Ph.D.
October 8, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP 1638

David T. Fox